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Optical Interferometry for Biology and Medicine

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Preface

Light is at once the most sensitive and the most gentle probe of matter. It is commonplace to use light to measure a picometer displacement far below the nanometer scale of atoms, or to capture the emission of a single photon from a fluorescent dye molecule. Light is easy to generate using light-emitting diodes or lasers, and to detect using ultrasensitive photodetectors as well as the now ubiquitous digital camera. Light also has the uncanny ability to penetrate living tissue harmlessly and deeply, while capturing valuable information on the health and function of cells. For these reasons, light has become an indispensible tool for biology and medicine. We all bear witness to the central role of light in microscopic imaging, in optical biosensors and in laser therapy and surgery.

Interferometry, applied to biology and medicine, provides unique quantitative metrology capabilities. The wavelength of light is like a meterstick against which small changes in length (or phase) are measured. This meterstick analogy is apt, because one micron is to one meter as one picometer is to one micron – at a dynamic range of a million to one. Indeed, a picometer is detected routinely using interferometry at wavelengths around one micron. This level of interferometric sensitivity has great utility in many biological applications, providing molecular sensitivity for biosensors as well as depth-gating capabilities to optically section living tissue.

Optical Interferometry for Biology and Medicine presents the physical principles of optical interferometry and describes their application to biological and medical problems. It is divided into four sections. The first provides the underlying physics of interferometry with complete mathematical derivations at the level of a junior undergraduate student. The basics of interferometry, light scattering and diffraction are presented first, followed by a chapter on speckle that gives the background for this important phenomenon in biological optics – virtually any light passing through tissue or cells becomes "mottled." Although it presents a challenge to imaging, speckle provides a way to extract statistical information about the conditions of cells and tissues. Surface optics is given a chapter to itself because of the central role played by surfaces in many optical biosensors and their applications.

The next three sections of the book discuss specific applications, beginning with interferometric biosensors, then interferometric microscopy followed by interferometric techniques for bulk tissues. Interferometric biosensors are comprised of many different forms, including thin films, waveguides, optical resonators and diffraction gratings. Microscopy benefits especially from interferometry because layers of two-dimensional cells on plates can be probed with very high sensitivity to measure subtle differences in refractive index of cells and their constituents. Quantitative phase microscopy has become possible recently through application of interferometric principles to microscopy. As cell layers thicken into tissues, imaging becomes more challenging, but coherent techniques like optical coherence tomography (OCT) and digital holography (DH) are able to extract information up to 1 mm deep inside tissue.

While the principles of interferometry are universal, this book seeks always to place them in the context of biological problems and systems. A central role is played by the optical properties of biomolecules, and by the optical properties of the parts of the cell. The structure and dynamics of the cell are also key players in many optical experiments. For these reasons, there are chapters devoted explicity to biological optics, including a chapter on cellular structure and dynamics as well as a chapter on the optical properties of tissues. Throughout the book, biological examples give the reader an opportunity to gain an intuitive feel for interference phenomena and their general magnitudes. It is my hope that this book will be a valuable resource for student and expert alike as they pursue research in optical problems in biology and medicine.

I would like to thank my current students Ran An, Karen Hayrapetyan and Hao Sun for proofreading the final manuscript, and much of this book is based on the excellent work of my former students Manoj Varma, Kwan Jeong, Leilei Peng, Ming Zhao and Xuefeng Wang. My colleagues Ken Ritchie, Brian Todd and Anant Ramdas at Purdue University provided many helpful insights as the book came together into preliminary form. Finally, I give my heartfelt appreciation to my wife Laura and son Nicholas for giving me the time, all those Saturday mornings, to do my "hobby."

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